## REMARKS

The present invention relates to methods for the treatment of a subject having an infirmity such as cancer. Invention methods are broadly applicable to the administration of a wide variety of pharmacologically active agents, and can be implemented by a variety of routes of administration. Invention methods comprise administering to a subject a sub-therapeutic dose level of a pharmacologically active agent (such as the anticancer agent paclitaxel) effective against a variety of cancers over an administration period sufficient to achieve a therapeutic effect.

By the present communication, claims 1, 7, 8, 15 and 17 have been amended to define Applicants' invention with greater particularity. This amendment does not introduce new matter as it is fully supported throughout the specification and claims as originally filed. In addition, in view of the amendments submitted herewith, claim 6 has been cancelled. Accordingly, Claims 1-5 and 7-21 are now pending in this application. The present status of all claims in the application is provided in the listing of claims presented herein beginning on page 2.

The Examiner's assertion that the specification allegedly does not contain an abstract of the disclosure is respectfully submitted to be in error. The present application is a 371 based on PCT Application No. US00/10849, the cover sheet of which contains an abstract of the disclosure. However, in order to reduce the issues and expedite prosecution, a replacement abstract is provided herewith.

The objection to informalities in claim 17 is noted, and has been obviated by the amendments submitted herewith.

**Rejection under 35 U.S.C. §112, first paragraph**

The rejection of claims 1-21 under 35 U.S.C. §112, first paragraph, is respectfully traversed.

Applicants respectfully disagree with the Examiner's assertion that "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims." (See page 3, lines 18-20 of the Office Action). This conclusion is based on an erroneous evaluation of the Wands factors by the Examiner, as follows.

**1) The nature of the invention** (see page 4 of the Office Action)

The Examiner has correctly characterized the invention.

**2) The state of the prior art** (see page 4 of the Office Action)

While the Examiner has correctly characterized the state of the prior art as having identified many different antineoplastic drugs, this observation actually supports Applicants' position that the claims are fully enabled. Applicants do not assert to have discovered any new antineoplastic agents—instead, Applicants have developed a new method of treatment, which is broadly applicable to any antineoplastic agent. The claimed method of treatment simply requires administration of any antineoplastic at sub-therapeutic dose levels (which could be readily identified by one of skill in the art) over a defined, extended period of time.

**3) The relative skill of those in the art** (see page 4 of the Office Action)

The Examiner correctly acknowledges that the level of skill of those in the relevant art is high.

**4) The predictability or unpredictability of the art** (see page 4 of the Office Action)

The Examiner's simple assertion that "[t]he unpredictability of the pharmaceutical and chemical art is high" (see page 4, line 18 of the Office Action) fails to consider the specific teachings of the present disclosure. The present claims are directed to a novel mode of delivery of known agents for their known activity; Applicants have discovered that an alternate mode of administration, relative to that taught in the prior art, is also effective with such compounds. Thus, when properly considered in the context of the present disclosure, i.e., in view of the findings disclosed herein, the question with respect to predictability of the art is more appropriately phrased in terms of whether it would be predictable to extrapolate from the demonstration provided herein with an exemplary pharmacologically active agent (i.e., one effective against a specific cancer being treated) to other pharmacologically active agents effective against the specific cancer being treated. Given the well known nature of these compounds, and the demonstrated utility of any one of them for the intended purpose, it is respectfully submitted that the operability of any other member of the group would be expected, with a high likelihood, to exhibit similar behavior in the same mode of treatment.

**5) The breadth of the claims** (see page 4 of the Office Action)

Applicants respectfully disagree with the Examiner's assertion that "[t]he claims are very broad..." (See page 4, line 20 of the Office Action). Contrary to the Examiner's assertion, the claims are drawn specifically to methods of treating cancer in a defined group of subjects (i.e., subjects exhibiting symptoms of cancer), employing a defined group of compounds (i.e., pharmacologically active agents effective against the specific cancer being treated) for such treatment.

**6) The amount of direction or guidance presented** (see page 5 of the Office Action)

The Examiner's assertion that "Applicant's specification does not provide guidance for the treatment of all types of cancers using 'any chemotherapeutic agent'" (see page 5, lines 2-3 of the Office Action) reflects a misconception as to the nature of the present invention. Contrary to

the Examiner's assertion, the claims are not directed to use of any chemotherapeutic agent. Instead, the claims, as amended, are directed to treatment of cancer using a pharmacologically active agent effective against the specific cancer being treated, employing a novel administration protocol.

Accordingly, it is respectfully submitted that the amount of direction or guidance provided by the present specification is commensurate in scope with the claims, as amended.

**7) The presence or absence of working examples** (see pages 5-6 of the Office Action)

There is no requirement that Applicants present any working examples to support the claimed invention. Indeed, even if there were no examples included in the specification, the present invention is submitted to be fully enabled by the present disclosure. The compounds appropriate to use are fully disclosed (i.e., pharmacologically active agents effective against the specific cancer being treated), as is the protocol for administration of such compounds.

Moreover, the specification provides an exemplary regimen for administration of a prototypical pharmaceutically active agent contemplated for use in the practice of the present invention (see Example 1 at page 18 of Applicants' specification). Nothing more is required.

**8) The quantity of experimentation necessary** (see page 6 of the Office Action)

In this section of the Office Action, the Examiner has provided no support for the assertion that "one of ordinary skill in the art would be burdened with undue experimentation to determine the chemotherapeutic compounds and sub-therapeutic dosages that would be capable of treating the large number of cancerous disorders encompassed by the claims." (See page 6, lines 10-13 of the Office Action). Contrary to the Examiner's assertion, no experimentation is required to determine the chemotherapeutic compounds that would be capable of treating the target cancer. Attention is directed to the language of claim 1, which requires "a pharmacologically active agent effective against the specific cancer being treated." What

experimentation is required for one of skill in the art to identify a compound as a member of this well defined class of compounds? None.

Similarly, no experimentation is required to determine sub-therapeutic dosages. Attention is directed to Applicants' specification at page 7, lines 9-26 where "therapeutic levels" and "sub-therapeutic dose levels" are defined. Since the claims are to be read in light of the specification, it is respectfully submitted that one of skill in the art has been fully informed what is contemplated by reference to "sub-therapeutic dosages."

In summary, it is respectfully submitted that the specification provides more than adequate enablement of the claimed methods. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 1-21 under 35 U.S.C. § 112, first paragraph.

**Rejections under 35 U.S.C. §102(b)**

The rejection of claims 1-4, 9-12, and 14-21 under 35 U.S.C. §102(b) as allegedly being anticipated by WO 94/06422 (Wilson et al.), is respectfully traversed.

Applicants' invention, as defined for example by claim 1, distinguishes over Wilson et al. by requiring treatment of a subject having cancer by administering to the subject a sub-therapeutic dose level of a pharmacologically active agent effective against the cancer, wherein the sub-therapeutic dose is administered over an extended administration time (e.g., in the range from about 7 days to about 1 year). Wilson et al. do not disclose or suggest such an administration protocol. In contrast, the "long term" administration of paclitaxel contemplated by Wilson et al. is no greater than 96 hours (barely half the minimum administration period of 7 days required by the present claims).

The rejection of claims 1-4, 6-11 and 13-21 under 35 U.S.C. §102(b) as allegedly being anticipated by Regazzoni et al (Comment in: Annals of Oncology 7(8):771-772 (Oct 1996), is respectfully traversed.

Applicants' invention, as defined for example by claim 1, distinguishes over Regazzoni et al. by requiring treatment of a subject having cancer by administering to the subject a sub-therapeutic dose level of a pharmacologically active agent effective against the cancer, wherein the sub-therapeutic dose is administered over an extended administration time (e.g., in the range from about 7 days to about 1 year). Regazzoni does not disclose or suggest such an administration protocol. Instead, Regazzoni teaches administration of 5-fluorouracil (as a third-line chemotherapy) at a daily dose of 250 $mg/m^2$, which is not a sub-therapeutic dose level.

**Rejections under 35 U.S.C. §103(a)**

The rejection of claims 5-8 and 13 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wilson et al., is respectfully traversed.

Applicants' invention, as defined for example by claim 5, distinguishes over Wilson et al. by requiring treatment of a subject having cancer by locally administering to the subject a sub-therapeutic dose level of a pharmacologically active agent effective against the cancer, wherein the sub-therapeutic dose is locally administered over an extended administration time (e.g., in the range from about 7 days to about 1 year). Wilson et al. do not disclose or suggest such an administration protocol. In contrast, Wilson et al. contemplate systemic (as opposed to local) administration of paclitaxel for no greater than 96 hours (barely half the minimum administration period of 7 days required by the present claims).

The rejection of claims 5 and 12 under 35 U.S.C. §103(a) as allegedly being unpatentable over Regazzoni et al. in view of Wilson et al., is respectfully traversed.

Applicants' invention, as defined for example by claim 5, distinguishes over Regazzoni et al. by requiring treatment of a subject having cancer by locally administering to the subject a sub-therapeutic dose level of a pharmacologically active agent effective against the cancer, wherein the sub-therapeutic dose is locally administered over an extended administration time (e.g., in the range from about 7 days to about 1 year). Instead, Regazzoni teaches systemic administration of 5-fluorouracil (as a third-line chemotherapy) at a daily dose of 250 mg/m$^2$, which is not local administration and is not administration at a sub-therapeutic dose level.

Further reliance on Wilson et al. is unable to cure the deficiencies of Regazzoni, since Wilson et al. suffers from the same limitations as the primary reference.

**Conclusion**

In view of the above amendments and remarks, prompt and favorable action on all claims is respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosure: Replacement abstract